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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,183	05/27/2005	Katharine S Ulmann	21101.0045U2	3496

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NEEDLE & ROSENBERG, P.C.
SUITE 1000
999 PEACHTREE STREET
ATLANTA, GA 30309-3915

EXAMINER	
SHAFER, SHULAMITH H	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,183	ULMANN ET AL.	
	Examiner	Art Unit	
	SHULAMITH H. SHAFER	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11,24-28,34,40,46,49-51,53,57,59 and 62* is/are pending in the application.

4a) Of the above claim(s) *1-3,11,24-28,34,40,46,49,51,53,57,59 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-3,11,24-28,34,40,46,49-51,53,57,59 and 62* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12 December 2005* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

Restriction Requirement:

Applicant's election, with traverse, of Group IX, claim 50, drawn to a method of inhibiting a cell cycle of a cell, in the reply filed on 12 October 2007 in response to Office Action of 12 April 2007 is acknowledged. The grounds for the traversal are that claim 28 (Group V), claim 34 (Group VI), claim 50 (Group IX), claim 51 (Group X), claim 53 (Group XI), claim 57 (Group XII) and claim 62 (Group XIV) relate to a single general inventive concept, as all of these claims deal with inhibiting Nup153. Additionally, applicant argues that Examiner has not established a search burden in examining all these groups in a single patent application.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

The requirement for restriction was made on an application entering the national stage as a 371 of PCT/US03/29267. Examiner determined that the inventions were not so linked as to form a single general inventive concept under PCT Rule 13.1, since the first claimed invention did not constitute a contribution over the prior art, therefore did not have a special technical feature and thus, could not share a special technical feature with the other claimed inventions. Furthermore, each of the inventions (Group V, VI, IX-XII and XIV) recite methods having different intended uses, goals, starting and ending points and require different method steps. It is noted that under 35 U.S.C. 121 and 372 Examiner need not demonstrate a search burden.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 1-3, 11, 24-28, 34, 40, 46, 49-51, 53, 57, 59, and 62 are pending in the instant application. Claims 1-3, 11, 24-28, 34, 40, 46, 49, 51, 53, 57, 59, and 62 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claim 50 is under consideration.

Information Disclosure Statement:

The information disclosure statement filed 12 December 2005 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because References A17-A19 recite Genbank accession numbers without indicating the date the sequences were deposited in the databanks. The databanks are constantly being updated; thus the sequences are not unambiguously identified. These references have been lined through and the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Rejections

35 U.S.C. § 112, Second Paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 50 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 50 is an incomplete method claim. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. To be complete, a method claim must state a goal in the preamble of the claim, and conclude having achieved that goal. Claim 50 is directed to a method of inhibiting a cell cycle of a cell. However, the method steps, as recited, are insufficient to accomplish the goal stated in

the preamble. The method steps recite administration of an inhibitor of Nup153. It is unclear if carrying out the method steps would result in accomplishing the goal set forth in the preamble.

Additionally, the claim is vague and indefinite in reciting "administering a Nup153 inhibitor to the cell". It is unclear if applicant intends administration to take place *in vivo* or *in vitro*.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 50 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of administering a Nup153 inhibitor to a cell *in vitro*, does not reasonably provide enablement for administering a Nup153 inhibitor to a cell *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claim recites a method of administering a Nup153 inhibitor to the cell. The language of the claim therefore encompasses administration to an isolated cell, and administration to a subject comprising said cell.

The specification teaches a method of inhibiting a cell cycle of a cell comprising administering a Nup153 inhibitor to the cell [paragraph 0297 of PGPUB 20050226879, the PGPUB of the instant application]. "Nup153 inhibitor" is not further identified or characterized in the disclosure. However, the disclosure teaches administration of compositions comprising molecules of different structural and functional characteristics to inhibit nuclear envelope breakdown [paragraph 0033]. The specification discloses that said inhibitors (of nuclear envelope breakdown) can also be used in methods of modulating Nup153 (interpreted as encompassing inhibition of Nup153 activity) and cell cycle progression [paragraph 0052]. Included among the inhibitors to be administered in the methods of the instant invention are:

Protein and protein fragments: a fragment encompassing the central zinc finger domain of Nup153 [paragraph 0038], variants of the Nup153 protein and Nup358 protein and derivatives of these proteins [paragraph 0140], chimeric proteins [paragraph 0191],

antibodies to Nup153 [paragraph 0051, 0160],

functional nucleic acids: antisense molecules, aptamers, ribozymes, triplex forming molecules, external guide sequences [paragraph 0087], RNA interference molecules (RNAi) or small interfering RNA (SiRNA) [paragraph 0092],

small molecules [paragraph 0192], such as flavenoids [paragraph 0194] and

synthetic peptides [paragraph 0359].

The specification teaches general methods of administration of compositions comprising inhibitors including electroporation, lipofection, calcium phosphate precipitation [paragraph 0116], uptake of naked DNA, liposome fusion, intramuscular injection of DNA via a gene gun, and endocytosis [paragraph 0123]. Additionally, the specification envisions delivery of nucleic acids either *in vitro* or *in vivo.* Methods of administration of compositions can largely be broken down into two classes: viral based delivery systems and non-viral based delivery systems [paragraph 0098]. The disclosure teaches compositions and methods can be used for targeted gene disruption and modification in any animal that can undergo these events, thus encompassing gene therapy methods [paragraph 0298].

Working examples: Examples 1 and 2 teach incubation of Nup153 fragments (Example 1) or synthetic peptides (13-meres) (Example 2) to cell free extracts derived from *Xenopus* eggs; these extracts form synthetic nuclei around sperm chromatin. There are no teachings, working or prophetic, of administration of inhibitors of Nup153 *in vivo*.

Administration of any of contemplated Nup153 inhibitors *in vivo* is not enabled for the following reasons:

It is well known in the art that the development and administration of pharmaceutical therapies are unpredictable (see for example, Goodman and Gilman, 10th edition, McGraw-Hill, 2001, page 3-29) for the following reasons: (1) the identified compound may be inactivated by degradation, immunological inactivation, or inherently short half-life before producing an effect; (2) the identified compound may not reach the target area; (3) individual differences in absorption, metabolism or excretion of identified compound; (4) other functional properties may make the identified compound unsuitable for *in vivo* therapeutic use (e.g. unacceptable toxic side effects). See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO BD. APP & Inter., 1992).

Additionally, the specification also envisions administration of nucleic acids as inhibitors of Nup153, that is, a method of gene therapy [for example, paragraph 0298]. However, the specification does not teach any methods or working examples of administration of nucleic acids *in vivo*. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be

required of the skilled artisan to introduce and express the claimed nucleic acid into the cell of an organism to inhibit the cell cycle. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express the claimed nucleic acid in the cell of an organism or be able to produce the encoded protein in that cell.

Due to the large quantity of experimentation necessary to introduce any of the recited molecules into a cell of an organism to inhibit the cell cycle, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of developing pharmaceutical therapies and the unpredictability of transferring nucleic acids into an organism's cells, and the breadth of the claims which fail to recite any limitations as to *in vitro* or *in vivo* methodologies, undue experimentation would be required of the skilled artisan to practice the claimed invention in its full scope.

Claim 50 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a **written description** rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims recite administration of a Nup153 inhibitor. This claim is drawn to a number of genera: compounds which inhibit Nup153.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or

she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117).

To provide adequate written description and evidence of possession of a claimed genus or claimed genera, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicant has identified t hecomposition to be administered only by description of a function, the ability to inhibit Nup153. However, the inhibitor is not further described by any common structural characteristics.

In the instant application, the specification discloses a wide variety of compounds of different structural and functional characteristics which may exhibit the required functionality: inhibition of Nup153. These compounds include, but are not limited to, a fragment encompassing the central zinc finger domain of Nup153 [paragraph 0038], variants of the Nup153 protein and Nup358 protein and derivatives of these proteins [paragraph 0140], chimeric proteins [paragraph 0191], antibodies to Nup153 [paragraph 0051, 0160], functional nucleic acids including antisense molecules, aptamers, ribozymes, triplex forming molecules, external guide sequences [paragraph 0087], RNA interference molecules (RNAi) or small interfering RNA (SiRNA) [paragraph 0092], small molecules [paragraph 0192], flavenoids [paragraph 0194] and synthetic peptides [paragraph 0359]. The specification teaches a single species of each of the following genera: variants of Nup153 (species: a fragment encompassing the central zinc finger domain of Nup153), antibodies (species: antibodies specific to Nup153), and synthetic

peptides (species: CTHPFTHECGGGS, SEQ ID NO: 30) as meeting the functional limitation stated in the claim.

Applicant has failed to provide any written description of most of the genera encompassed by the claim (variants of the Nup153 protein Nup358 protein and derivatives of these proteins, chimeric proteins, and functional nucleic acids including antisense molecules, aptamers, ribozymes, triplex forming molecules, external guide sequences, RNA interference molecules (RNAi) or small interfering RNA (SiRNA), small molecules) and has only provided adequate description of a single species within each of three broad genera, as discussed above.

Claim 50 is thus a single means claim wherein the claim covers every conceivable structure (means) for achieving the stated purpose (inhibiting a cell cycle) but the specification at most discloses only three compositions.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genera, which are inhibitors of Nup153. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genera. Therefore, only the following compounds: a fragment encompassing the central zinc finger domain of Nup153, antibodies specific to Nup153, and the synthetic peptide of SEQ ID NO:30 but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 50 is rejected under 35 U.S.C. 102(b) as being anticipated by Shah et al (1998. Current Biology 8:1376-1386, cited on IDS, reference A45).

The claim is drawn to a method of inhibiting a cell cycle by administration of Nup153. “A method of inhibiting a cell cycle" is recited as intended use in the preamble of the claim and is thus given minimal patentable weight. Shah et al teach administration of fragments of Nup153 which act as dominant-negative inhibitors of Nup153 (abstract). Among the fragments administered are those comprising the zinc finger domains of Nup153 (Nup153-N’ and Nup153-Zn (page 1379, 2nd column, 2nd paragraph). The specification of the instant invention teaches that fragments comprising a zinc finger domain acts as a Nup153 inhibitor. Thus, the teachings of Shah et al anticipate the limitations of Claim 50.

Conclusion:

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lorraine Spector/
Primary Examiner, Art Unit 1647

/S. H. S./
Examiner, Art Unit 1647